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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/402,707 10/08/99 HOUTHOFF H 570-28

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HM22/0322

EXAMINER

SISSON, B

ART UNIT

PAPER NUMBER

1655

11

DATE MAILED: 03/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/402,707

Applicant(s)

HOUTHOFF ET AL.

Examiner

Bradley L. Sisson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/8/01, 2/14/01 and 3/1/01.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-105 is/are pending in the application.
- 4a) Of the above claim(s) 51-105 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claims 23-105 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.
2. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.
3. In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 23-50, drawn to a method for labeling a nucleotide.

Group II, claim(s) 51-54, drawn to a labeled nucleotide.

Group III, claim(s) 55-79, drawn to a method of labeling a nucleotide.

Group IV, claim(s) 80-105, drawn to a labeled substance having formula VII.

4. The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds can have differing linkers, nucleotide sequences and formula compositions.
5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.
6. During an in-person conversation with Irving N. Feit, Reg. No. 28,601, on 01 March 2001 a provisional election was made without traverse to prosecute the invention of Group I, claims 23-50. Affirmation of this election must be made by applicant in replying to this Office action. Claims 51-105 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

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7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

8. The use of the trademark TWEEN (e.g., TWEEN 20 as found at page 19, line 4) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

9. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue

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experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided and The Presence or Absence of Working

Examples

The specification has been found to provide guidance for (i) the preparation of a labeled 5-AA-dUTP (page 16) and (ii) plasmid DNA labeling and purification (page 18). At page 16 of the specification it is disclosed that $[\text{Pt}(\text{en})(\text{BioDadoo-NH}_2)(\text{NO}_3)](\text{NO}_3)$ was used and at page 18 it is disclosed that BioDadoo-ULS was used. The specification discloses at page 14, lines 29-30, that BioDadoo was purchased from Boehringer Mannheim. The specification does not disclose just what constitutes BioDadoo nor how such a compound is made. Normally, the commercial availability of a compound would not lead to the need for greater enablement, however, in the present case, Boehringer-Mannheim Biochemicals no longer exists (merged with Roche) and the product is not commercially available. Accordingly, the specification does not set forth in sufficient detail the reaction conditions and starting materials required to practice the claimed

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invention. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42

USPQ2d 1001. As set forth in the decision of the Court:

While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

"It is true . . . that a specification need not disclose what is well known in the art. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

In the present case the specification had unfortunately relied upon the continued commercial availability of an essential starting material in order to satisfy the enablement requirement as set forth under 35 USC 112, first paragraph. Through merger and the apparent withdrawal from market the only disclosed source of the essential starting material, and with no other like product having been disclosed, the specification does not satisfy the enablement requirement.

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

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In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The prior art, while disclosing the use of an aliphatic diamine, is essentially silent as it relates to the use of BioDadoo.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

The claims have sufficient breadth of scope so to encompass an immense number of compounds. The compounds can vary not only in terms of the linker used, be it for X, A, and/or B, but also in terms of the nucleotide or polynucleotide attached. The specification, however, discloses the development of but two compounds. In support of this position, attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a “written description of the invention” which is separate and distinct from the enablement requirement. The purpose of the “written description” requirement is broader than to merely explain how to “make and use”; the “applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the “written description” inquiry, *whatever is now claimed*.

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Attention is also directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; *In re Wahlforss et al.*, 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

11. While the present claims are drawn to the production of a class of compounds and not to the compounds *per se*, the specification, through the disclosure of the manufacture of but two compounds, does not disclose a generic method by which the entire family of compounds can be prepared sans the skilled artisan having to resort to undue experimentation, assuming *arguendo*, that the BioDadoo compound were still commercially available or the specification were to disclose how such a compound could have been made and utilized in the instantly claimed method.

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12. For the above reasons, and in the absence of convincing evidence to the contrary, the specification has not been found to enable the claimed method and as such, claims 23-50 are rejected under 35 USC 112, first paragraph.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

14. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

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17. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in cursive script, appearing to read "B. L. Sisson".

Bradley L. Sisson
Primary Examiner
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BLS
March 19, 2001